Amendments to the Drawings:

The attached sheets of drawings includes changes to Figs. 1A-1D and 2A-2C. Also attached are annotated copies of the drawings marked by hand to show the changes made.

The sheet that includes Fig. 1, replaces the original sheet including Fig. 1. The amended Fig. 1 moves the NHCOR" moiety so that the N is beneath the bond marker.

The sheet that includes Fig. 2A corrects the formula shown in the window so as to correct the sphingosyl moiety shown at the lower right so as to change the O to an OH and to add a double bond. Also, the C to the left of the CH group was changed to CH_2. Finally the O in the palmitoyl group in the upper right of the formula was changed to a C.

The sheet that includes Fig. 2B corrects the formula shown in the window so as to correct the O_2H group on the left of the formula to be an O_2N group.

The sheet that includes Fig. 2C corrects the formula shown in the window so as to correct the sphingosyl moiety shown at the lower right so as to change the CH to an OH and to add a double bond.

Attachment: Replacement Sheets of Figs. 1A-1D and 2A-2C.
Annotated Sheets showing changes.

REMARKS

Claims 30-39, 41-50, 52-55 and 59 presently appear in this case. Claims 50 and 52-55 have been withdrawn from consideration. Claims 30-39 and 59 have been allowed. Claims 40 and 49 have been objected to and claims 41-49 have been rejected. The Official Action of February 25, 2009, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to novel sphingoid-polyalkylamine conjugates, a process for their preparation, a process for use, and pharmaceutical compositions comprising the same.

In the Official Action of February 25, 2009, the examiner erroneously indicated that non-elected claims 51-55 were no longer in the case. That is not true. Applicant's amendment of September 19, 2008, as supplemented by applicant's supplemental amendment of December 12, 2008, clearly left claims 50-55 in the case and traversed the restriction requirement. The examiner has ignored applicant's traversal and has not responded thereto. Accordingly, reconsideration and withdrawal of the restriction requirement is again respectfully urged. As the examiner has never responded to applicant's traversal of the restriction requirement and as the restriction requirement has never been

made final, consideration of this traversal must be given and a new official action issued.

In applicant's amendment of September 19, 2008, applicant pointed out that the examiner erred in making a restriction requirement under 35 U.S.C. §121 when the present application was a national stage application and a unity of invention requirement under 37 CFR §1.499 and PCT Rule 13 should have been made; see MPEP 1893.03(d). The examiner's reasons for requiring restriction, as previously provided, are totally irrelevant to unity of invention considerations. In order to clarify that the compositions contain the compounds of claim 30 and that the method of use is for using the compound of claim 30, the withdrawn claims have now been amended to delete the long recitation of the formula and to simply refer to claim 30. Clearly, the compound of claim 30 is the special technical feature which is common to all of the claims. Particularly as claim 30 has now been allowed, the method of use of this compound must be rejoined, considered and allowed, regardless of the grounds for original restriction.

Accordingly, in view of the fact that all of the present claims have the same special technical feature which defines over the prior art, reconsideration and withdrawal of

the restriction requirement and examination of all of the claims now present in the case are respectfully urged.

Claims 41-49 have been rejected under 35 U.S.C. §112 because the term "activating agent" in claim 41 is a relative term which renders the claim indefinite. The examiner states that the term is not defined by the claim and one of ordinary skilled in the art would not be reasonably apprised of the scope of the invention. This rejection is respectfully traversed.

As was previously pointed out, the term "activating agent" is defined at page 12 of the present specification. For purposes of clarification, page 12 of the specification has now been amended to specify that the activating groups are "for hydroxyl-containing molecules." As it is clear from step (b) of the process that the activating agents are to obtain an activated OR_3 and/or OR_4 group, step (b) has also been clarified to specify that, rather than obtaining an activated R_3 and/or R_4 group, an activated OR_3 and/or OR_4 group is obtained. None of these changes comprise proscribed new matter, as the specification specifically contains reference to the literature with respect to activating groups and specifically Hermanson "Bioconjugate Techniques", *Academic Press* (1996), pages 142 and 183. These pages have been previously made of record. It can be seen that on page 142,

lines 7-4 from the bottom of the page, the disuccinimidyl carbonate is used "to activate hydroxyl-containing molecules." See also page 183 at the second and third lines of the first paragraph where it states that CDI "can activate… hydroxyl groups for conjugation with other nucleophiles". In the starting material for making the compounds of formula I, one or both of OR_3 and OR_4 are hydroxyl groups. Accordingly, these amendments to the specification are merely for clarification and do not add any new matter.

Claim 41 has been similarly amended to specify that the activating agent is an "agent for activating the hydroxy moieties of OR_3 and/or OR_4" and to specify that it is activated "OR_3 and/or OR_4 group" that is obtained. Accordingly, as presently amended, the term "activating agent" is no longer relative or indefinite. The amended language defines exactly what the group activates and the specification shows that such groups for activating hydroxyl moieties are well known in the art and that those of ordinary skill in the art would know what groups to use in order to activate a hydroxyl group of a molecule. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claim 40 has been objected to because the structure contains CH instead of CH_3 and claim 49 has been objected to

because it is not clear how the amide group is attached to the polyalkylamine chain.

Claims 40 has now been deleted as being duplicative in scope with claim 39, which claims the same compound by name. The chemical structure of this compound is also shown in Fig. 2C (see the first paragraph on page 7 of the present specification). This figure has now been corrected to correct the errors in the chemical structure therein, as will be discussed below.

Claim 49 has now been amended to obviate this rejection. In claim 49, the formulae have now been corrected to show that the NHCOR" moieties are connected to the remainder of the structure through their N atom, as obviously intended.

With respect to claim 40, With respect to claim 49,

Similarly, the drawings have now been amended to correct errors noted therein. Claims 1A, 1B, 1C and 1D have been amended in the same manner as has now been done in claim 49, as discussed above, to correct the point of attachment of the NHCOR" groups.

Fig. 2A has been amended to correct the formula shown in the window so as to correct the sphingosyl moiety shown at the lower right so as to change the O to an OH and to add a double bond. Also, the C to the left of the CH group

was changed to CH_2. The examiner was incorrect in criticizing the same structure in previously appearing claim 40, stating that the CH group should be CH3. The error was that the CH group should have been an OH group. Furthermore, a double bond was omitted from the sphingosyl moiety. Submitted herewith is the "metabocard" for "sphingosine" in the Human Metabolome Database (http://www.hmdb.ca/metabolites/HMDB00252). It shows the chemical structure for sphingosine (also known as D-erythro-sphingosine). It can be seen that the hydroxy group and the double bond in sphingosine are as in the corrected formula in corrected Fig. 2A (and in corrected Fig. 2C to be discussed below). The specification, in the first paragraph on page 7, connects the name with the chemical structure in Figs. 2A and 2C. Also, the C to the left of the CH group was changed to CH_2. Finally the O in the palmitoyl group in the upper right of the formula was changed to a C.

The chemical name of the compound in Fig. 2A is given in the first paragraph on page 7 of the specification, thereby confirming that the group at the upper right is palmitoyl and that at the lower right is sphingsyl. Accordingly, the structure shown now corresponds to the name and the empirical formula given in Fig. 2A, as well as the

exact mass and mol. wt. given. Accordingly, these corrections do not include new matter, but merely correct clerical errors.

Fig. 2B has been amended to correct the structure to change the O_2H group shown on the far left to O_2N as was obviously intended, as the group is specified at the first paragraph of page 7 as being a trinitrophenyl moiety. Again, no new matter is involved in making this correction.

Fig. 2C has been amended to correct the chemical structure shown in the window so as to change the CH to an OH and to add a double bond in the sphingosyl group shown in the lower right of the formula (see the discussion of Fig. 2A above). Accordingly, the corrections to the chemical structure shown in Fig. 2C do not include new matter, for the same reasons as discussed above with respect to the corrections to the sphingosyl moiety in Fig. 2A.

Reconsideration and withdrawal of the rejection of claim 49 and entry of all of these corrections to the drawings are therefor respectfully urged.

The examiner's indication of allowability of claims 30-39 and 59 are gratefully acknowledged.

It is submitted that all of the claims now present in the case clearly define over the references of record and

fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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